Citation:

Cobo E. Effect of different doses of ethanol on the milk-ejecting reflex in lactating women. *Am J Obstet Gynecol.* 1973; 115 (6): 817-821.

PubMed ID: 4688584

Study Design:

Non-randomized trial

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effect of different doses of ethanol on the milk-ejection reflex in lactating women.

Inclusion Criteria:

- Healthy women who are breastfeeding
- Normal delivery between two and eight days before the study.

Exclusion Criteria:

- Men
- Women who are not breastfeeding
- Women who had a complicated delivery.

Description of Study Protocol:

Recruitment

Not stated.

Design

Non-randomized trial.

Intervention

- 10 minutes of baby's suckling was the stimulus used to evoke the milk-ejecting reflex
- Measurement of the milk-ejecting activity was completed and this served as the control value
- 10 minutes of baby's suckling was repeated

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- Alcohol was infused on a gram per kilogram body weight basis
- 10 minutes of baby's suckling was repeated immediately after stopping the alcohol infusion
- Measurement of the milk-ejecting activity was taken
- Two subjects also had uterine motility simultaneously recorded
- Single intravenous doses of synthetic oxytocin were given to all women.

Statistical Analysis

- Estimation of milk-ejecting reflex
    - Correlation coefficient between the alcohol blood level and the dose administered was calculated
    - Area under the intramammary pressure curve tracings and the latency of the response were the parameters used to measure the reflex
    - Expressed in square millimeters and seconds, respectively
    - Mean values were obtained along with the standard error of the mean
    - P-values were calculated for statistical significance.

Data Collection Summary:

Timing of Measurements

- To stimulate the milk-ejecting reflex, the infant suckled for 10 minutes and the milk-ejecting response was recorded which served as a control
- Alcohol was then infused with a grams per kilogram body weight dose
- 10 minutes of the infant's suckling was repeated immediately after stopping the alcohol infusion
- Oxytocin doses were repeated during and after the alcohol infusion.

Dependent Variables

- Area of the milk-ejecting response
    - Recorded by means of intravital pressure recordings
    - Planimetrically measuring of the area under the intramammary pressure curve tracings during the suckling period
    - Measured in square millimeters
- Latency of the milk-ejecting response
    - Time that elapsed between the starting of suckling and the beginning of the response
    - Measured in seconds.

Independent Variables

- Ethyl alcohol intake
    - Expressed in weight per volume
    - For analysis, the data was separated into four groups based on dose
        - 0.10 to 0.49
        - 0.5 to 0.99
        - 1.0 to 1.49
        - 1.5 to 1.99
        - Two subjects received more than 2.0g per kg.

Control Variables

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- Intravenous oxytocin was provided to all women
    - A dose-effect relationship was determined
- Uterine motility was recorded in two subjects
    - Simultaneously recorded by using a microballoon connected through polyethylene tubing to a transducer and a recording unit.

Description of Actual Data Sample:

- *Initial N:* 40 women
- *Attrition (final N):* 40 women
- *Age:* Not stated
- *Ethnicity:* Not stated
- *Anthropometrics:* Not provided
- *Location:* Colombia, South America.

Summary of Results:

Key Findings

- Doses of ethanol of 0.147 to 0.937g per kg body weight were not associated with a significant change in the milk-ejecting response
- Doses of ethanol of 1.021 to 1.480g per kg
    - Average area of the response (mm^2):
        - Control: 1,220
        - After alcohol: 449 ($P<0.02$)
    - Average latency of the response (seconds):
        - Control 73
        - After alcohol: 369.4 ($P<0.001$)
- Doses of ethanol of 1.583g per kg
    - Average area of the response (mm^2)
        - Control: 1,143
        - After alcohol: 224 ($P<0.001$)
    - Average latency of the response (seconds):
        - Control: 38.2
        - After alcohol: 330.8 ($P=0.01$)
- Percentage of change in milk-ejecting responses after alcohol administration showed that:
    - Doses 0.14 to 0.49g per kg did not decrease activity
    - Doses 0.5 to 0.99g per kg decreased activity by 18.2%
    - Doses 1.0 to 1.49g per kg decreased activity by 63.2%
    - Doses 1.5 to 1.99g per kg decreased activity by 80.4%.

Other Findings

The correlation coefficient between ethyl alcohol blood concentration and the dose administered was 0.92.

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Dose of Ethanol (g/kg)	Number of Subjects	Area of the Response (mm^2)		Latency of the Response (seconds)	
		Control	Experimental	Control	Experimental
0.147-0.450	7				
Range		610-2,700	500-2,990	18-60	20-120
Average		1,173	1,323	39.8	48
SEM		271	314	6.08	13
P-Value		<0.8		<0.6	
0.521-0.937	8				
Range		950-2,340	0-1,970	12-440	24-600
Average		1,356	1,111	59.9	176.7
SEM		166.5	238.4	25.9	86.3
P-Value		<0.4		0.2	
1.021-1.48	14				
Range		400-3,850	0-1,970	12-440	24-600
Average		1,220	449	73	369.4
SEM		253	162.7	29.1	63.5
P-Value		<0.02		<0.001	
1.583	9				
Range		600-3,490	0-640	18-80	40-600
Average		1,143	224	38.2	330.8
SEM		238.4	78.2	6.2	86.5
P-Value		<0.001		0.01	
2.038	1	820	370	42	246
2.507	1	250	0	24	600

Blocking of milk-ejecting reflex

- Group receiving 0.521 to 0.937g per kg of alcohol (eight women):
  - One had complete block of the milk-ejecting reflex
  - Two had partial block
  - Five had no inhibition
- Group receiving 1.021 to 1.464g per kg of alcohol (14 women):
  - Six had complete block of the milk-ejecting reflex
  - Seven had partial block
  - One had no inhibition
- Group receiving 1.583 to 1.924g per kg of alcohol (nine women):
  - Three had complete block of the milk-ejecting reflex
  - Six had partial block
- One woman received 2.507g per kg of alcohol and had a complete block of the milk-ejecting

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reflex
- One woman received 2.038g per kg of alcohol and had a partial block of the milk-ejecting reflex.

Uterine motility

Uterine motility was measured in two women: No constant uterine responses were recorded in spite of mammary gland activation.

Percentage change in milk-ejecting response

Percentage of change in milk-ejecting responses after alcohol administration showed that:

- Doses 0.14 to 0.49g per kg did not decrease activity
- Doses 0.5 to 0.99g per kg decreased activity by 18.2%
- Doses 1.0 to 1.49g per kg decreased activity by 63.2%
- Doses 1.5 to 1.99g per kg decreased activity by 80.4%.

Oxytocin effect

There was no difference in response of the mammary gland to injected oxytocin under normal conditions and under the influence of alcohol.

Author Conclusion:

Inhibition of the milk-ejecting response occurs in women in a dose-dependent relationship are dependent on ethanol levels. The inhibition begins at ethanol doses higher than one gram per kilogram.

Reviewer Comments:

- *The authors state that additional information on the study design was reported in a previous article*
- *Five tracings of the intramammary and uterine motility are reproduced in this article*
- *Unclear whether the number of subjects included in the study is sufficient.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes

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4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	No
2.	**Was the selection of study subjects/patients free from bias?**	No
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	No
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	No
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	No
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	???
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	No

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4.1.	Were follow-up methods described and the same for all groups?	No
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	No
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A

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7.	**Were outcomes clearly defined and the measurements valid and reliable?**		Yes
	7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
	7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
	7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
	7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
	7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
	7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		???
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	No
	8.2.	Were correct statistical tests used and assumptions of test not violated?	No
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	No
	8.6.	Was clinical significance as well as statistical significance reported?	No
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		No
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	No
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes

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